Distal radius bone microarchitecture: what are the differences between age 25 and old age?

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Conflict of Interest:

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Abstract

Summary This study reported that the transitional zones in older adults were enlarged at the expense of the compact-appearing cortex with a greater in porosity in all cortical sub-compartments. The magnitude of differences in areal and volumetric bone mineral density (aBMD, vBMD) between older and younger groups were similar.

Introduction Aging is strongly associated with bone loss, but little is known about magnitudes of differences in bone microarchitectures, aBMD and vBMD from peak bone mass (PBM) to senescence. We aimed to describe differences in aBMD, vBMD and bone microarchitecture parameters at the distal radius between older and young adults.

Methods We compared 201 participants, aged 62-89 years (female 47%) and 196 participants, aged 24-28 years (female 38%). Bone microarchitecture parameters at distal radius were measured using high-resolution peripheral computed tomography (HRpQCT). aBMD was measured using dual energy X-ray absorptiometry (DXA). Unpaired t-tests and chi square tests were used to compare differences in means and proportions as appropriate.

Results Older adults had thinner compact-appearing cortices with larger (cross-sectional area: outer 30.96mm^2 vs. 28.38mm^2, inner 36.34mm^2 vs. 32.93mm^2) and thicker (outer 0.57mm vs. 0.54mm, inner 0.71mm vs. 0.65mm) transitional zones compared to young adults (all $p<0.05$). Cortical porosity was modestly higher in older adults than in young adults (54% vs. 49%, $p<0.001$). The magnitude of the difference in hip aBMD between older and young adults was slightly lower than of total radial vBMD (-0.51 SD vs. -0.78 SD).

Conclusion Compared with young adults at the time of PBM, the transitional zones in older adults were enlarged at the expense of the compact-appearing cortex with a greater porosity in all cortical sub-compartments. The similar SD differences in aBMD and vBMD between older and younger groups suggest that the differences in bone area are not leading to major artefactual change in aBMD.

Keywords: Bone microarchitecture; Bone mineral density; High-resolution peripheral quantitative computed tomography; Peak bone mass

Introduction

Osteoporotic fracture is a growing public health problem and a major cause of death in the aging population (1, 2). Peak bone mass (PBM) and subsequent bone loss are both important contributors to fracture risk in later life (3). Aging is strongly associated with significant bone loss in both sexes (4), with evidence that areal bone mineral density (aBMD) declines by 12%-30% in both sexes from age 20 to 80 years (5). Therefore, knowing the magnitude and patterns of bone loss from PBM to senescence is important for understanding fracture and identifying populations at high risk of fracture.

Dual energy X-ray absorptiometry (DXA) has long been the gold-standard for diagnosing osteoporosis and predicting fracture (6) but has limitations. The measured aBMD is calculated by dividing average bone mass by area, as a 2-dimensional structure, which is blind to the spatial distribution of the mineralized bone. Thus, aBMD could increase if total bone mass increases more relative to bone area such as in osteoarthritis (5, 7, 8), while vBMD may be constant or lower as the bone thickness increases. This might explain why most studies show an increase in spine aBMD with age suggesting the increase in area negates the decrease in bone mass. In addition, DXA cannot provide other information on bone factors that contribute to bone strength, such as structural design, trabecular and cortical material composition.

High-resolution peripheral quantitative computed tomography (HRpQCT) measures cortical and trabecular bone microarchitecture at peripheral sites (9). Bone microarchitecture changes have been assessed in menopausal women (10-12) and in older men (13), as has the heritability of bone microarchitecture (14). However, there are few studies comparing differences in bone microarchitecture assessed using HRpQCT in adults at the time of PBM to later life. One cross-sectional study measured bone microarchitecture by HRpQCT at the distal radius in people aged from 20 to 90 years (15), but estimated bone outcomes at age 90 based on modelling rather than direct comparison of bone parameters in the elderly with those at PBM. Additionally, there was a lack of analysis in cortical subcompartments including compact cortical bone, outer and inner transitional zone bone.

Therefore, the aim of this study was to compare bone microarchitecture parameters in a sample of adults at the time of PBM with those in a sample of older adults, and to compare the differences in vBMD to those in aBMD in the same populations.

Materials and Methods

Participants

This study was conducted by comparing data from two population-based studies, the he Tasmanian Older Adult Cohort (TasOAC) study and the T-bone study. TASOAC is a prospective, population-based cohort study, for which adults aged between 50 and 79 years in 2002 were selected from the electoral roll in Southern Tasmania (population 229,000) using sex-stratified random sampling. The overall response rate was 57%. Participants were excluded if they were institutionalized or had contraindications to magnetic resonance imaging (MRI). Baseline data (phase 1) were collected between February 2002 and September 2004 in 1099 participants. The current study consisted of a convenience consecutive sample of 201 participants who had HRpQCT parameters measured between 2013 and 2014 (phase 4). The study was approved by the Southern Tasmanian Health and Medical Human Research Ethics Committee, and written informed consent was obtained from all participants. T-bone is a Tasmanian birth cohort study from 1988 and 1989. There were 13,592 live births in Tasmania during this time. At the time of birth, a scoring system was used to select infants at higher risk of sudden infant death syndrome (SIDS) as possible participants in an infant health study (16). From these, 1500 infants who were born in Southern Tasmania were enrolled in the T-bone study. Follow-up data were collected between 2004 and 2005 in 415 participants. This study analyzed data from 196 participants at age 25 years who were follow up between August 2013 and September 2015. The Southern Tasmanian Health and Medical Human Research Ethics Committee approved the study, and all participants provided written informed consent.

Anthropometry and other factors

Name, date of birth, and sex were recorded in a questionnaire during an interview. Standing height was measured to the nearest 0.1cm (bare feet) using a stadiometer. Body weight was measured to the nearest 0.1 kg using calibrated electric scales (without shoes, socks, and bulky clothing). Body mass index (BMI) was calculated as weight/height^2 (kg/m^2).

Areal bone mineral density (aBMD) assessments

The same DXA (Discovery W, Hologic, Bedford MA, USA) was used to scan the lumbar spine, total hip, and femoral neck during 2013-2015 for both samples and determine areal bone mineral density (aBMD). The coefficient of variations for our machine in 2013-15 using daily measurements of a spine phantom was 0.48%.

Bone microarchitecture measurement at distal radius

HRpQCT (Xtreme CT, Scanco Medical, Bruttisellen, Switzerland) was used to scan the distal radius in all participants. The region of interest of 9.02mm (110 CT slices) was at the standardized distance of 9.5 mm from the manually positioned reference line at the end plate of the distal radius. Acquired images were analyzed using StrAx1.0 (StraxCorp, Melbourne, Australia) (16). StrAx1.0 analysis is limited to the proximal 49 slices where cortices at the thickest allowing a more robust quantification of porosity. The compact-appearing cortical areas, outer and inner transitional zones, and trabecular compartments were segmented. Total, cortical, and trabecular cross-sectional area of selected slices, vBMD, porosity within the total cortex and its compartments, cortical thickness (Ct.Th), trabecular bone volume fraction (Tb.BV/TV), number (Tb.N), thickness (Tb.Th) and separation (Tb.Sp), and matrix mineral density were quantified. The segmentation algorithm is an automated method of segmentation of bone from background and bone into its compact-appearing cortex, transitional zone, and trabecular compartment is described, with a new approach to quantification of cortical porosity, which is achieved by automatically selecting attenuation profile curves perpendicular to the periosteal surface (17). The accuracy, reproducibility errors and the segmentation algorithm are fully described in the patent (18). The reproducibility errors for segmentations and quantification of porosity expressed as root mean square coefficients of variation ranged from 0.54% to 3.98% and were <1.5% for vBMD.

Statistical analysis

Older (n=201) and young participant's (n=196) general characteristics, DXA and HRpQCT bone parameters are presented as means and standard deviations (SD) or number (%).

SD difference (standardized using the means and SD at the time of PBM) of bone parameters between total older and younger adults, older and younger males and females was calculated.

All analyses were performed using Stata V.15.0 (StataCorp LP). Two-tailed p value <0.05 was considered as statistically significant.

Results

There were 201 older (107 males and 94 females) and 196 young adults (122 males and 74 females) included. Table 1 presents anthropometric characteristics and HRpQCT parameters of participants. Height was less in older adults, but other anthropometric characteristics were similar within the two cohorts. Compared to young adults, older adults had larger and thicker outer and inner transitional zone bone, and smaller and thinner

compact cortical bone. Cross-sectional area for total, cortical and trabecular bone, and thickness of cortical and trabecular bone were similar in younger and older adults. Older adults also had lower vBMD at all compartments with the largest SD difference being for the outer transitional zone, higher porosity at the cortical and transitional zones, and lower Tb.BV/TV with more separated trabecular structure and lower Tb.N than young adults. The SD difference between older and younger adults in spine aBMD was smaller than that for radial vBMD at all sites but this difference was not statistically significant. The magnitudes of differences in aBMD at total hip and femoral neck were similar albeit slightly lower than compact cortical and outer transitional zone vBMD at the distal radius. These differences remained statistically significant after adjustment for height (data not shown).

Table 2 shows the comparison of bone parameters between older age and the age of PBM by sex. Older males had larger cross-sectional area of total, cortical, transitional zone and trabecular bone, and thicker cortical and transitional zone bone, compared with the younger sample. Amongst females, the older age sample had larger cross-sectional area at the transitional zone and of trabecular but not cortical bone, thicker inner transitional zone bone, smaller and thinner compact cortical bone, compared with the younger sample. Older males and females both had lower vBMD at all compartments, higher prevalence of porosity, lower Tb.N and more separated trabecular structure than their younger counterparts.

Figures 1(a-d) illustrate the differences in bone parameters between the different ages for males and females. In males, the largest SD difference in bone geometry vBMD and porosity were all in outer transitional zone (Figure 1a-c), and the largest SD difference in trabecular microarchitecture was Tb.Sp (Figure 1d). However, in females, the largest SD difference of bone geometry was compact cortical bone area (Figure 1a). Similar to males, the largest SD differences in female vBMD and porosity were both outer transitional zone (Figure 1b-c). The largest SD difference in trabecular microarchitecture was Tb.N (Figure 1d).

The ratios of the area in each compartment to total bone area are shown as Figure 2. Compared with younger age, the ratios of cortical area and trabecular area to total bone area were 0.01 higher and 0.01 lower respectively in older age (Figure 2a). The ratios of transitional zone area (both outer and inner transitional zone) to total bone area was 0.02 higher in older than in younger age, with the ratio of compact cortical bone area to total bone area 0.03 lower in older than in younger age (Figure 2a). Within in the total cortex, compared with young adults at age of PBM, the ratios of outer and inner transitional zone area to cortical bone area were 0.02

and 0.03 higher respectively in older adults, with the ratio of compact cortical bone area to cortical bone area 0.05 lower in older adults (Figure 2b).

Discussion

This cross-sectional study compared differences in bone geometry, vBMD, prevalence of porosity, and trabecular structure parameters between adults at the time of PBM and older adults. The magnitude of differences in aBMD at total hip and femoral neck between young adults at age of PBM and older adults were broadly similar to vBMD at the distal radius, suggesting that differences in bone area may not lead to major artefactual change in aBMD. Differences in ratios of cortical subcompartments area to total cortex imply pathways for the enlargement in transitional zone area with aging.

The limitations of DXA could lead to artefactual changes in aBMD which disguise true bone density change and may lead to underestimation of fracture risk in older age (5, 19-21), especially at sites with significant bone area change. Technically, DXA cannot directly measure true bone density, as aBMD is calculated by bone mass divided by bone cross-sectional area. Previous studies have confirmed that bone area is not linearly associated with bone volume and aBMD is strongly influenced by bone area, therefore suggesting that aBMD change with age will only be accurate if bone size remains constant (22-24). Our results at the radial metaphysis indicate that is not the case with an increased bone size (particularly at the transitional zone bone area) and thickness in both sexes, which is consistent with studies at other sites (21, 25). In addition, DXA cannot distinguish and capture cortical and trabecular compartment parameters. Given this, we expected that magnitude of differences in bone density between older and younger adults at clinically significant sites would be lower using DXA compared with vBMD. However, the current study provides direct evidence that magnitude of age differences in aBMD at the hip (but not spine) were only slightly lower than of vBMD at the distal radius.

The differences in bone microarchitecture parameters between age groups were similar in males and females, apart from bone geometry parameters. Notably, there were differences in cross-sectional area and thickness at compact cortical bone and transitional zone bone from PBM to later life. Both older males and females had larger and thicker transitional zone bone, but older females also had smaller and thinner compact cortical bone. This is not surprised as previous longitudinal studies confirmed that women losing more bone with higher rates of bone loss than men with ageing (26, 27). This can be partly explained by differences in intracortical and

endocortical resorption in males and females during ageing (21, 28), and provides further supports of the view that periosteal apposition during senescence is greater in males than in females (29, 30).

Age differences in the ratios of cortical subcompartments area shed light on the mechanisms responsible for the enlargement of transitional zones at the expenses of the compact cortical bone. Previous cross-sectional and longitudinal studies regarding "trabecularization" have described the increment of trabecular size at expenses of thinning total cortex (31-33), but this neglects changes within the total cortex. We used a new method which allows accurate and reproducible segmentation of the transitional zone from inner cortex and trabeculae (17). The ratio of transitional zone to total cortex was higher with a lower ratio of compact cortical bone to total cortex with aging. Overlooking differences within cortical subcompartments thus may underestimate bone loss and the estimating the ratio of transitional zone and ratios of the compact cortical bone may improve fracture-risk prediction (34).

The current study has potential limitations. Firstly, our study design was cross-sectional and did not report on changes in matched individuals followed for many years. Thus, these results may be affected by possible cohort effects or change in population bone mass over time. Hip fracture rates are decreasing in Australia, so this is a possibility (35). However, while long-term longitudinal data would be preferable, it will be some time before such studies can be completed given that HRpQCT is a recent development. Secondly, this study had two different sampling frames, one being population-based via the electoral roll (TASOAC) and one being from a birth cohort selected to be at high risk of sudden infant death syndrome (T-Bone). However, both studies were chosen from the southern Tasmanian population and had comparable characteristics, suggesting this may not be a substantial issue when comparing these groups. Thirdly, our study only has HRpQCT parameters at distal radius. We did not have HRpQCT parameters at tibia in TASOAC, but significant correlations in bone microarchitectures have previously been reported between two peripheral sites (36). Fourthly, some clinical variables were not measured in both studies (e.g. race/ethnicity, tobacco and alcohol use, steroid exposure, diabetes, other medical issues might be relevant to bone loss). Thus, we are unable to compare these between the two age groups. Fifthly, in this study, younger adults were originally selected from infants considered at higher risk for SIDS. This might have an influence on the generalizability of this cohort to the general infant population. However, the participants' aBMD at age 25 was comparable with other studies in healthy populations of similar age and reference values for adulthood (37-39) suggesting that our result might not have been affected by this bias. Lastly, the socioeconomic and nutritional status were not available in these studies, which might bias the

difference of bone measures between two age groups because of attaining PBM in different decades with potential secular trends.

In conclusion, compared with young adults at the time of PBM, the transitional zones in older adults were enlarged at the expense of the compact-appearing cortex with a greater porosity in all cortical sub-compartments. The largest SD difference was in outer transitional zone vBMD. The similar SD differences in aBMD and vBMD between older and younger groups suggest that the differences in bone area are not leading to major artefactual change in aBMD.

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Table 1 Participants' characteristics and bone parameters measured by HRpQCT

	Older adults (n=201)	Young adults (n=196)	SD difference	P-value
Age (years)	72.22 (6.51)	25.50 (0.72)		
Female (%)	47	38		0.069
Height (cm)	166.78 (8.64)	177.32 (9.45)		<0.001
Weight (kg)	77.45 (12.52)	80.57 (19.40)		0.189
BMI (kg/m^2)	27.85 (4.08)	27.00 (5.62)		0.229
Current smokers (%)	5	20		<0.001
Age at menarche (years)	12.97 (1.43)	12.76 (1.25)		0.34
Asthma (%)	14	34		<0.001
Geometry				
Tt.Ar (mm^2)	286.46 (72.36)	275.12 (69.06)	0.16	0.111
Ct.Ar (mm^2)	106.93 (23.73)	105.25 (18.83)	0.09	0.436
Compact Cortical Ar (mm^2)	39.63 (12.51)	43.95 (10.53)	-0.41	<0.001
Outer TZ Ar (mm^2)	30.96 (6.85)	28.38 (5.10)	0.51	<0.001
Inner TZ Ar (mm^2)	36.34 (8.96)	32.93 (8.07)	0.42	<0.001
Tb.Ar (mm^2)	179.53 (53.73)	169.87 (54.46)	0.18	0.076
Ct.Th (mm)	1.96 (0.31)	1.97 (0.26)	-0.04	0.695
Compact Cortical Thickness (mm)	0.68 (0.20)	0.78 (0.20)	-0.50	<0.001
Outer TZ Thickness (mm)	0.57 (0.10)	0.54 (0.06)	0.50	<0.001
Inner TZ Thickness (mm)	0.71 (0.10)	0.65 (0.08)	0.74	<0.001
vBMD (mg HA/cm^3)				
Tt.vBMD	370.73 (80.70)	424.57 (69.11)	-0.78	<0.001
Ct.BMD	734.51 (88.98)	801.04 (67.53)	-0.99	<0.001
Compact cortical vBMD	928.57 (84.57)	991.24 (58.85)	-1.06	<0.001
Outer TZ vBMD	899.29 (72.57)	959.52 (44.74)	-1.35	<0.001
Inner TZ vBMD	385.47 (59.09)	408.34 (49.49)	-0.46	<0.001
Tb.vBMD	144.19 (59.72)	178.02 (51.29)	-0.66	<0.001
Microarchitecture				
Cortical porosity (%)	54 (7)	49 (5)	1.04	<0.001
Compact cortical porosity (%)	39 (7)	34 (5)	1.05	<0.001
Outer TZ porosity (%)	42 (6)	37 (4)	1.25	<0.001
Inner TZ porosity (%)	82 (4)	81 (3)	0.38	<0.001
Tb.N (mm^{-1})	3.26 (0.61)	3.66 (0.46)	-0.86	<0.001
Tb.Th (mm)	0.19 (0.01)	0.19 (0.01)	0.00	0.673
Tb. Connectivity	0.79 (0.25)	0.94 (0.24)	-0.60	<0.001
Tb. Separation (mm)	1.12 (0.28)	0.94 (0.22)	0.81	<0.001
Tb.BV/TV (%)	5 (3)	6 (2)	-0.53	<0.001
Matrix mineral density (%)	68 (1)	67 (1)	0.59	<0.001
aBMD (g/cm^2)				
Spine aBMD	1.04 (0.19)	1.06 (0.12)	-0.21	0.157
Total Hip aBMD	0.95 (0.15)	1.02 (0.13)	-0.51	<0.001
Femoral Neck aBMD	0.77 (0.12)	0.90 (0.13)	-1.00	<0.001

All values are means (standard deviation) unless otherwise stated. SD: standard deviation; Tt.Ar: total cross-sectional area; Ct.Ar: total cortical area; TZ Ar: transitional zone bone area; Tb.Ar: trabecular area; Ct.Th: total cortical thickness; Tt.vBMD: total volumetric bone density; Ct.vBMD: total cortical volumetric bone density; Tb.vBMD: trabecular volumetric bone density; TZ.vBMD: transitional zone bone volumetric bone density; Tb.N: trabecular number; Tb.Th: trabecular thickness; Tb.BV/TV: trabecular bone volume fraction; HA: hydroxyapatite. aBMD: areal bone mineral density. *P*-value<0.05 presents statistical significance.

Table 2 Bone measures between older and young males, and older and young females

	Males		Females	
	Older (n=107)	Young (n=122)	Older (n=94)	Young (n=74)
Geometry				
Tt.Ar (mm^2)	335.59 (56.00)†	307.76 (61.62)	230.54 (41.82)	221.32 (41.60)
Ct.Ar (mm^2)	124.50 (15.42) †	115.41 (14.97)	86.94 (13.45)	88.51 (10.93)
Compact cortical Ar (mm^2)	47.69 (9.35)	48.79 (9.13)	30.47 (8.80)‡	35.96 (7.39)
Outer TZ Ar (mm^2)	35.79 (4.91)†	31.08 (4.17)	25.46 (3.99)‡	23.93 (2.88)
Inner TZ Ar (mm^2)	41.02 (7.98)†	35.54 (7.75)	31.01 (6.79)‡	28.62 (6.67)
Tb.Ar (mm^2)	211.09 (47.63)†	192.35 (52.07)	143.60 (34.25)‡	132.81 (34.52)
Ct.Th (mm^2)	2.14 (0.25)†	2.06 (0.25)	1.76 (0.23)	1.81 (0.18)
Compact Cortical Thickness (mm)	0.77 (0.17)†	0.84 (0.20)	0.58 (0.18)‡	0.69 (0.16)
Outer TZ Thickness (mm)	0.62 (0.09)†	0.57 (0.61)	0.51 (0.08)	0.50 (0.04)
Inner TZ Thickness (mm)	0.74 (0.10)†	0.66 (0.08)	0.67 (0.09)‡	0.63 (0.08)
vBMD (mg HA/cm^3)				
Tt.vBMD	389.57 (73.96)†	430.86 (68.48)	349.28 (83.04)‡	414.20 (69.37)
Ct.vBMD	751.49 (77.12)†	800.73 (61.37)	715.18 (97.66)‡	801.54 (77.07)
Compact Cortical vBMD	930.91 (74.17)†	977.19 (50.74)	925.92 (95.38)‡	1014.41 (64.12)
Outer TZ vBMD	908.40 (63.54)†	951.71 (39.74)	888.92 (80.74)‡	972.40 (49.59)
Inner TZ vBMD	404.55 (57.06)†	422.71 (47.56)	363.75 (53.86)‡	384.64 (43.35)
Tb.vBMD	167.77 (54.58)†	198.21 (46.36)	117.35 (53.91)‡	144.73 (40.74)
Microarchitecture				
Cortical Porosity (%)	53 (6)†	49 (5)	56 (8)‡	49 (6)
Compact cortical porosity (%)	39 (6)†	35 (4)	40 (8)‡	32 (5)
Outer TZ porosity (%)	41 (5)†	37 (3)	43 (7)‡	36 (4)
Inner TZ porosity (%)	80 (4)	79 (3)	83 (4)	82 (3)
Tb.N (mm^{-1})	3.49 (0.44)†	3.78 (0.41)	3.00 (0.68)‡	3.45 (0.45)
Tb.Th (mm)	0.19 (0.01)	0.19 (0.01)	0.18 (0.01)	0.18 (0.01)
Tb. Connectivity	0.90 (0.22)†	1.04 (0.20)	0.68 (0.23)‡	0.78 (0.21)
Tb. Separation (mm)	1.02 (0.21)†	0.88 (0.18)	1.23 (0.31)‡	1.05 (0.22)
Tb.BV/TV (%)	6 (3)†	7 (2)	4 (2)	4 (2)
Matrix mineral density (%)	68 (1)†	67 (1)	68 (1)‡	67 (1)

All values are means (standard deviation). Tt.Ar: total cross-sectional area; Ct.Ar: total cortical area; TZ Ar: transitional zone bone area; Tb.Ar: trabecular area; Ct.Th: total cortical thickness; Tt.vBMD: total volumetric bone density; Ct.vBMD: total cortical volumetric bone density; Tb.vBMD: trabecular volumetric bone density; TZ vBMD: transitional zone bone volumetric bone density; Tb.N: trabecular number; Tb.Th: trabecular thickness; Tb.BV/TV: trabecular bone volume fraction; HA: hydroxyapatite. † Denotes statistical significance between older and young males. ‡ Denotes statistical significance between older and young females.

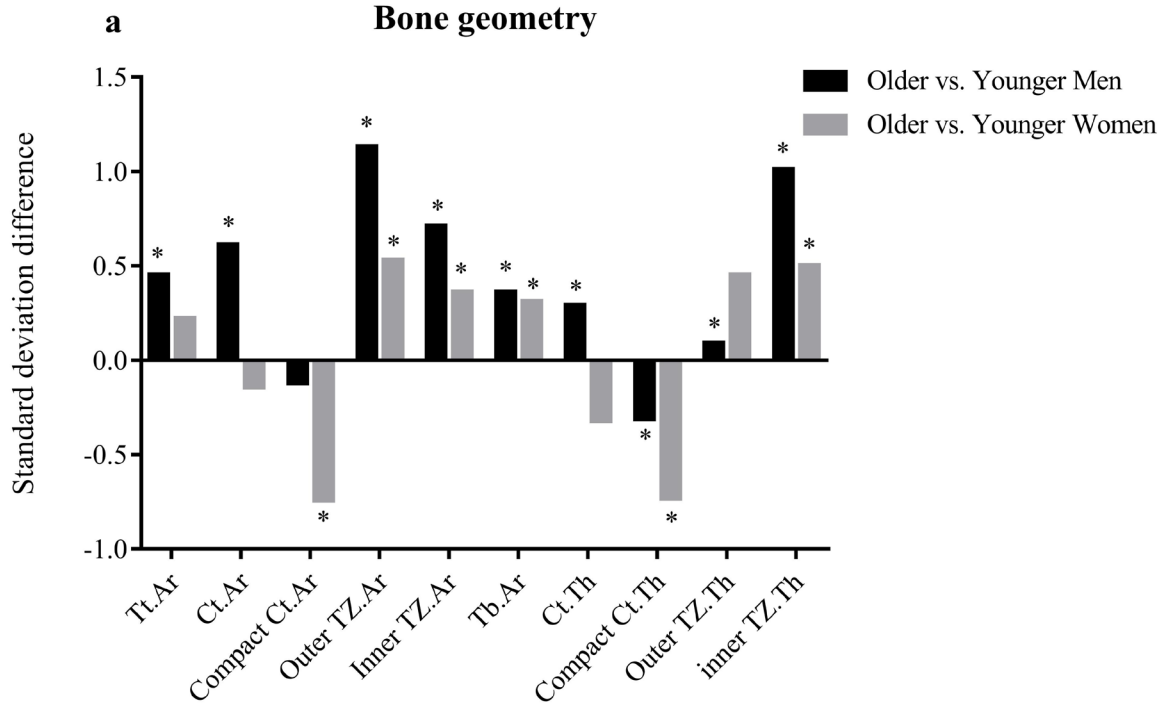

Fig. 1a Standard deviation difference in bone geometry between older and younger groups for each sex. Tt.Ar: total cross-sectional area; Ct.Ar: total cortical area; TZ.Ar: transitional zone bone area; Tb.Ar: trabecular area; Ct.Th: total cortical thickness; TZ.Th: transitional zone bone thickness. * Denotes statistical difference between older and younger groups in the same sex.

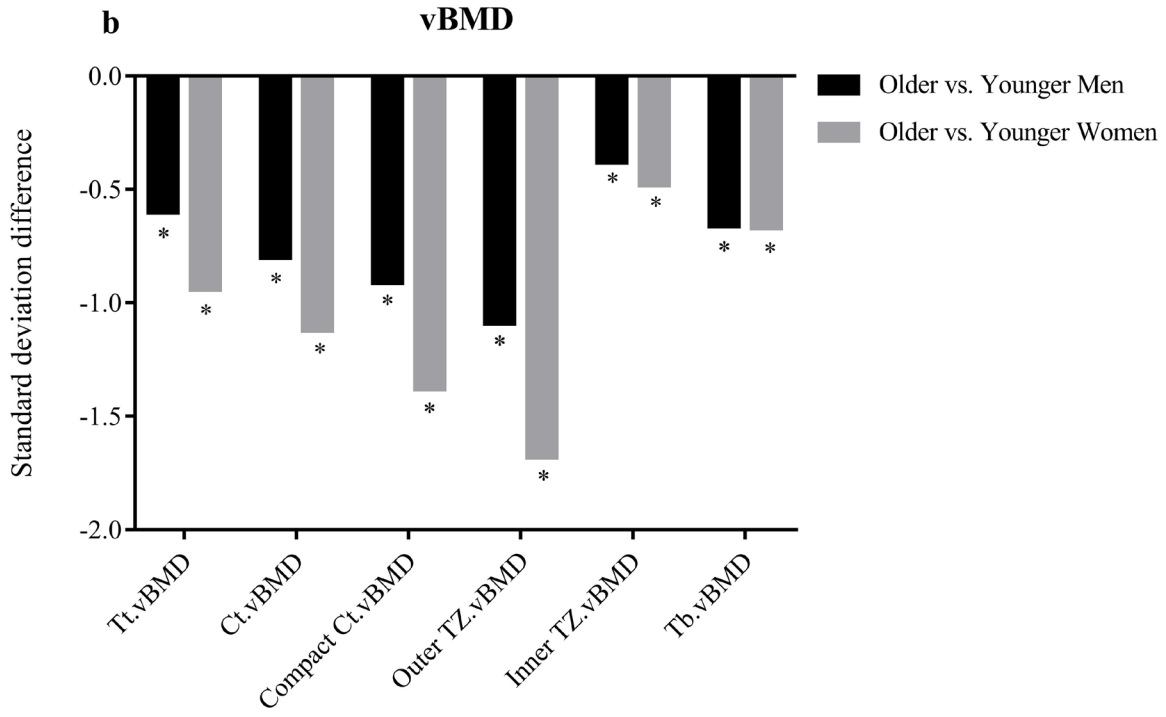

Fig. 1b Standard deviation differences in bone vBMD between older and younger groups for each sex. Tt.vBMD: total volumetric bone density; Ct.vBMD: volumetric bone density of total cortex; TZ.vBMD: volumetric bone density of transitional zone bone; Tb.vBMD: trabecular volumetric bone density. * Denotes statistical difference between older and younger groups in the same sex.

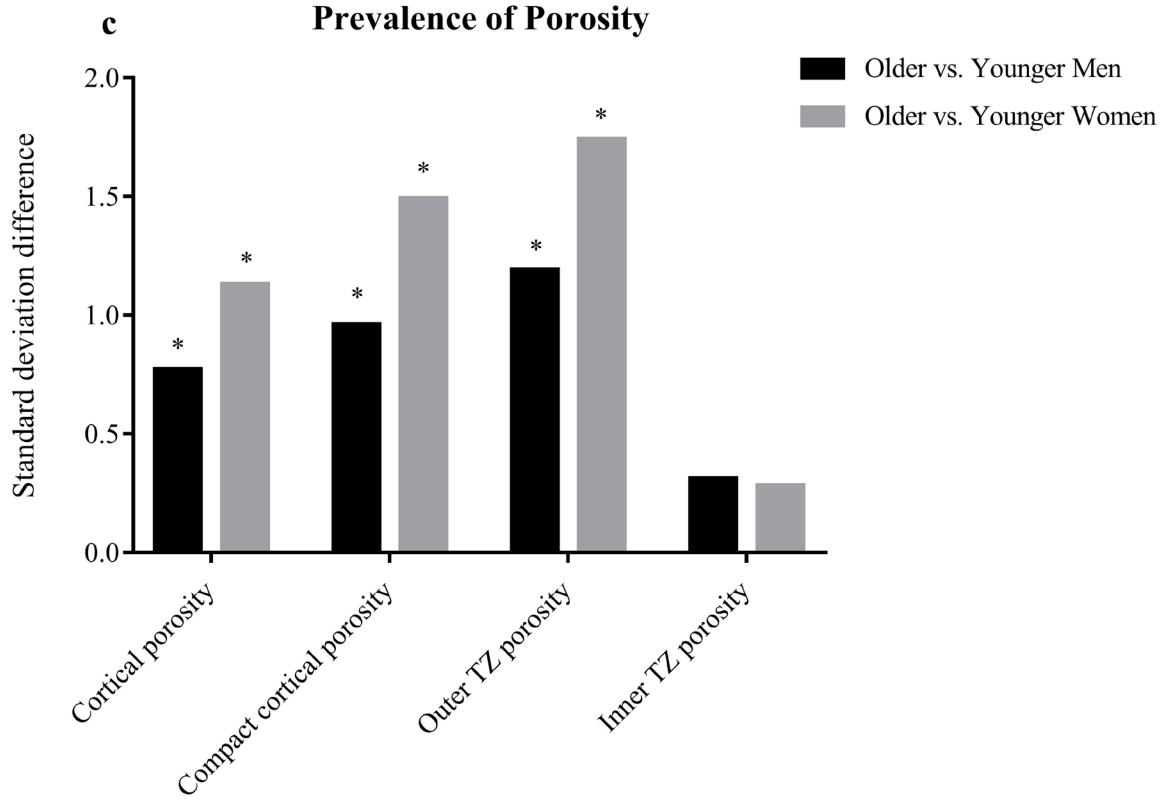

Fig. 1c Standard deviation differences in prevalence of porosity between older and younger groups for each sex. TZ: transitional zone bone. * Denotes statistical difference between older and younger groups in the same sex.

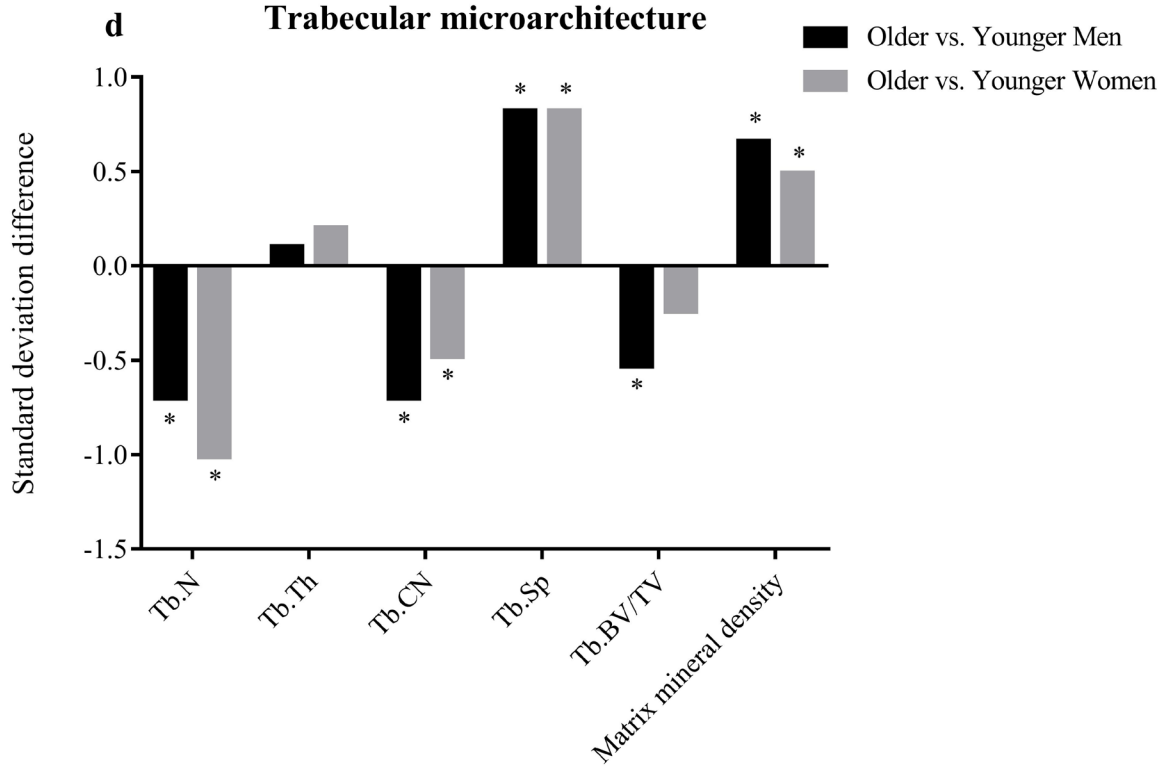

Fig. 1d Standard deviation differences in trabecular microarchitecture between older and younger groups for each sex. Tb.N: trabecular number; Tb.Th: trabecular thickness; Tb.CN: trabecular connectivity; Tb.Sp: trabecular separation; Tb.BV/TV: trabecular bone volume fraction. * Denotes statistical difference between older and younger groups in the same sex.

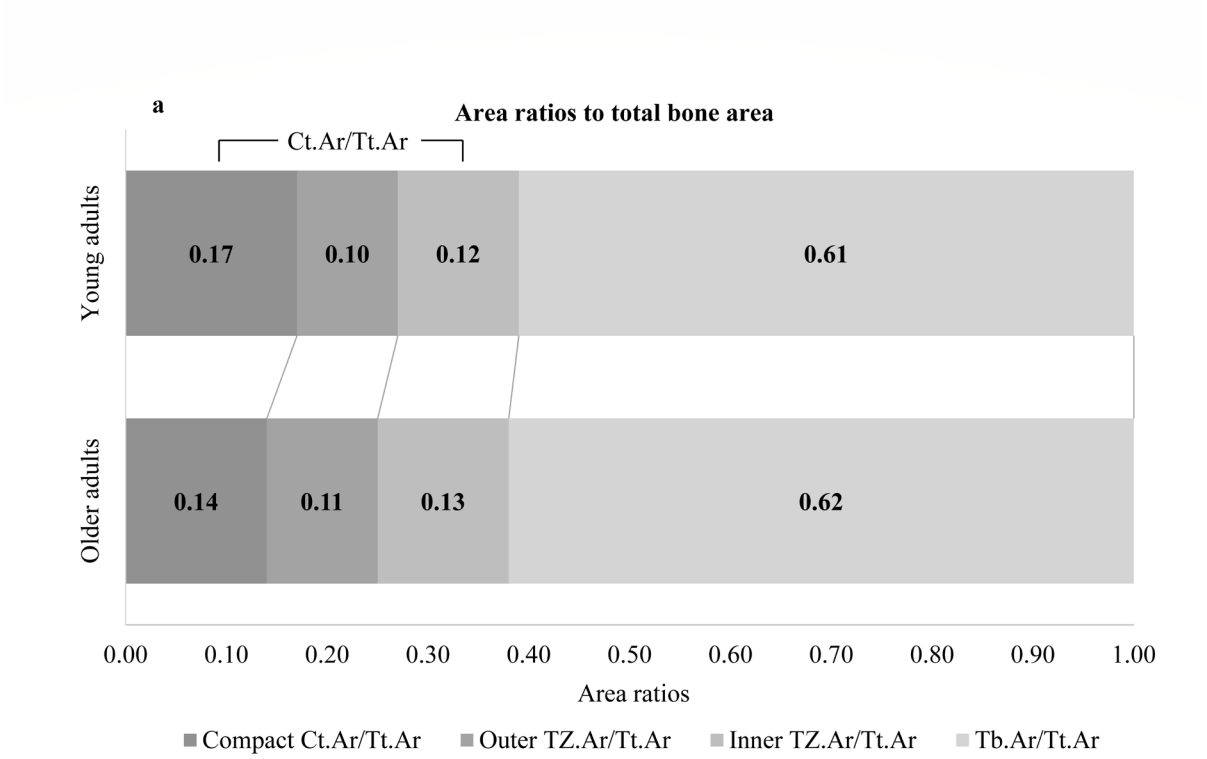

Fig. 2a The cross-sectional area ratios to total bone area. Tt.Ar: total cross-sectional area; Ct.Ar: cortical area; TZ.Ar: transitional zone bone area; Tb.Ar: trabecular area. Tt.Ar = Ct.Ar + Tb.Ar; Ct.Ar = Compact Ct.Ar + Outer TZ.Ar + Inner TZ.Ar. Bold denotes statistical significance between older and young adults.

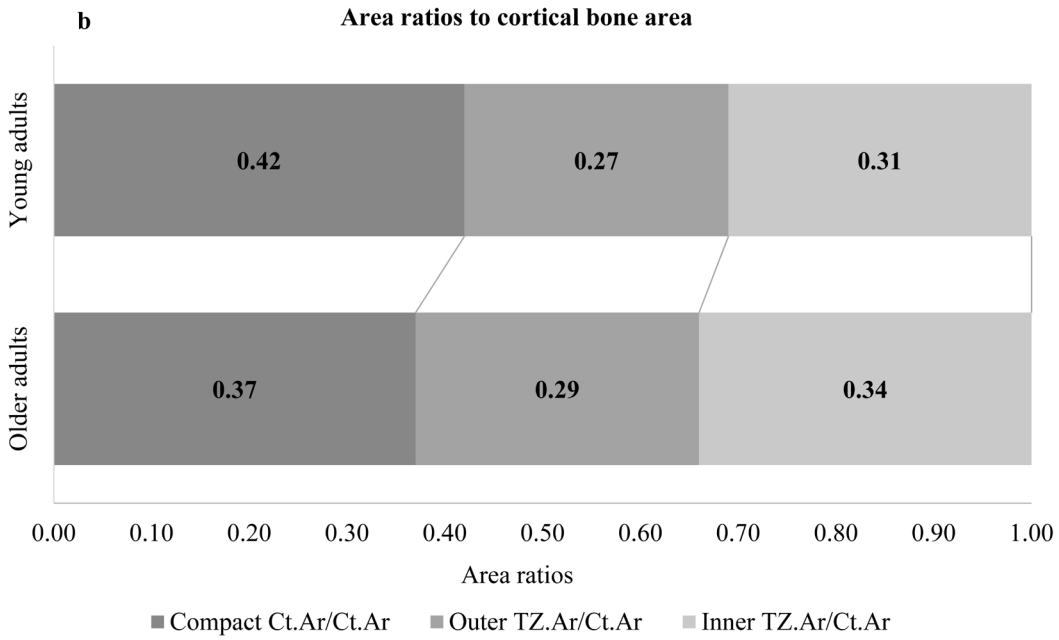

Fig. 2b The cross-sectional bone area ratios to the total cortical bone area. Ct.Ar: cortical area; TZ.Ar: transitional zone bone area; Tb.Ar: trabecular area. Ct.Ar = Compact Ct.Ar + Outer TZ.Ar + Inner TZ.Ar. Bold denotes statistical significance between older and young adults.